



# **Armed Forces College of Medicine**

## **AFCM**



# **Tumor Immunology**

**Wrap up session**

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Immunology**

## INTENDED LEARNING OBJECTIVES (ILO)



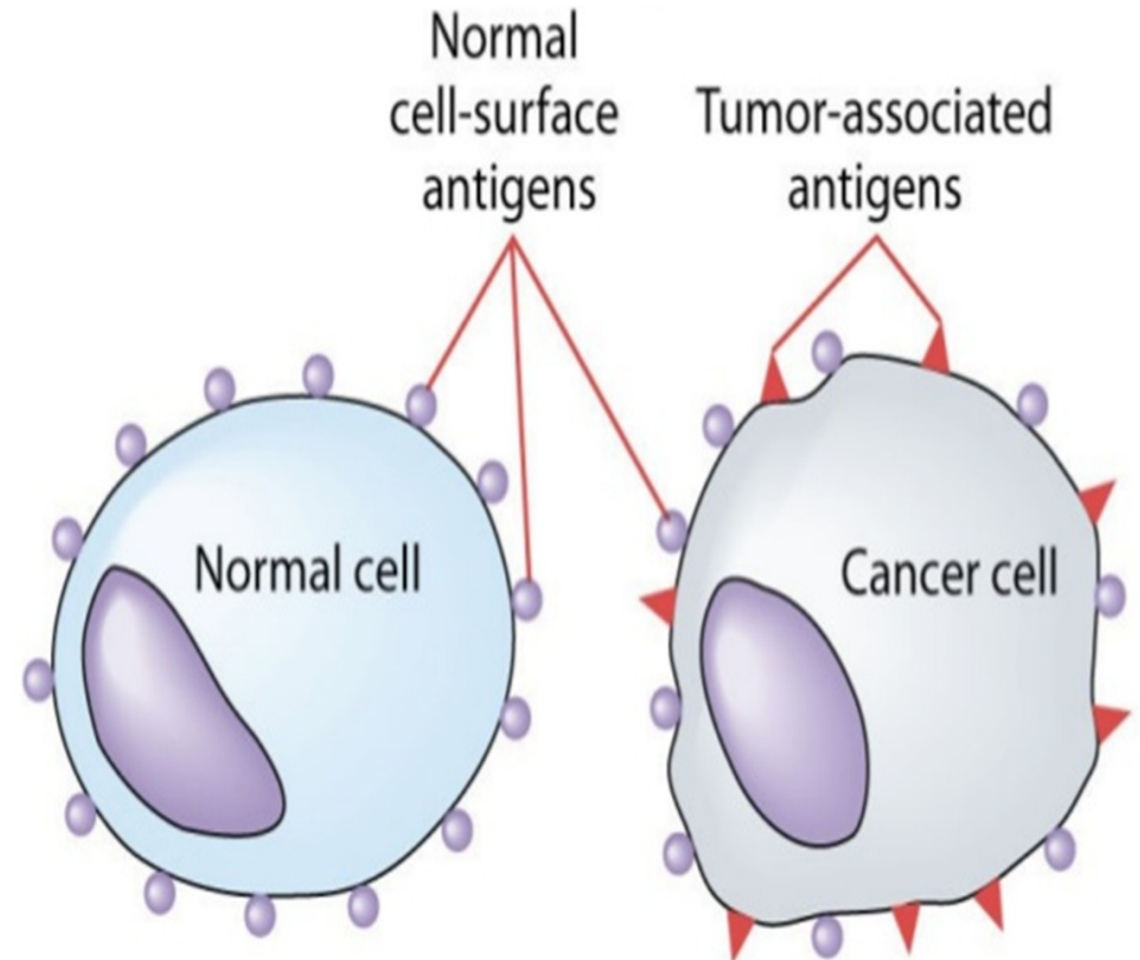
**By the end of this session the student will be able to:**

- 1. Define tumor antigens and outline examples**
- 2. Outline immune surveillance theory**
- 3. Mention the diagnostic and prognostic role of tumor markers .**
- 4. Explain mechanisms by which tumors evade the immune response of the host**
- 5. Identify the approaches for tumor immune therapy**

# Tumor Antigens



**How can tumor antigens be classified?**



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# Tumor Antigens

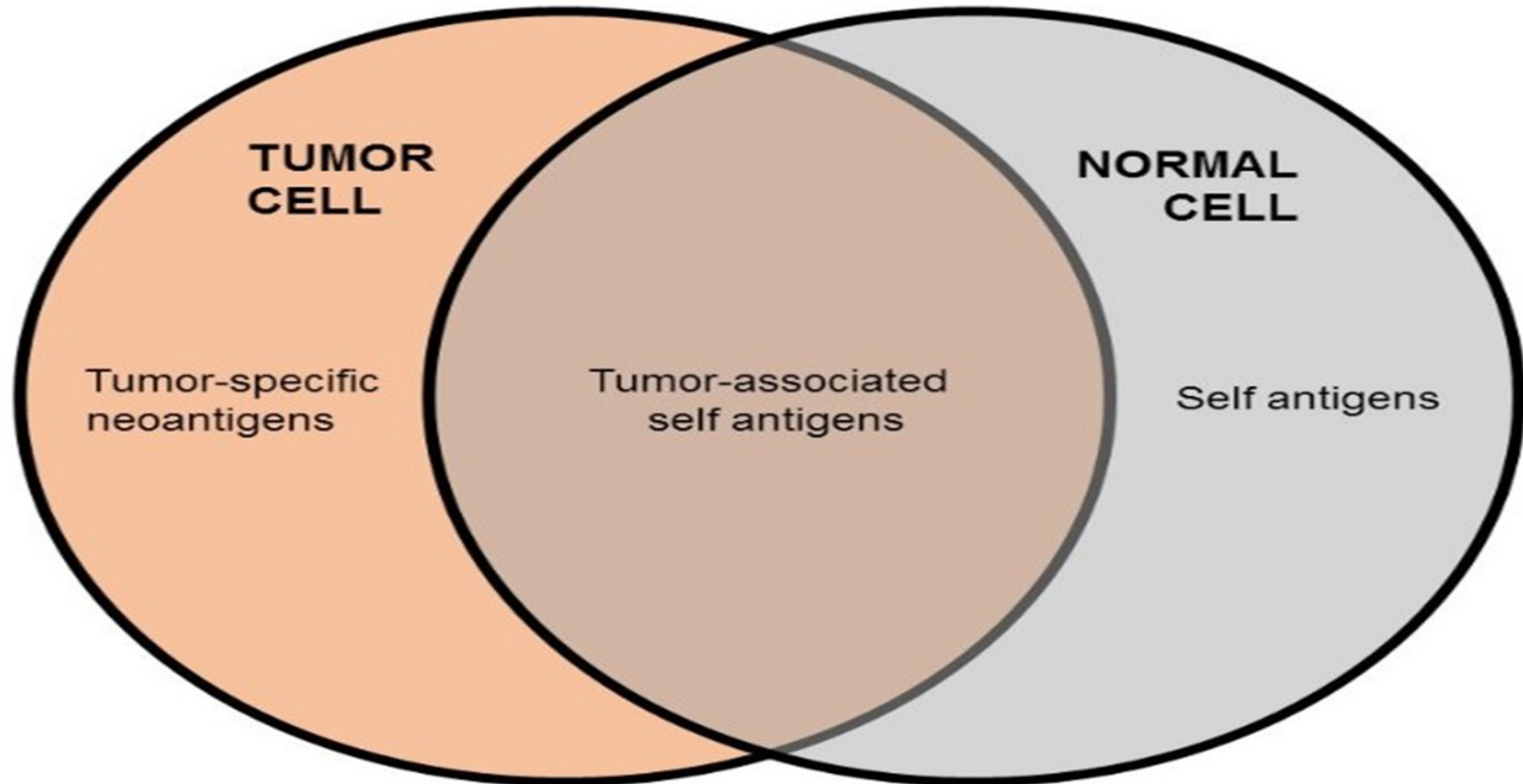


- I. according to pattern of expression:

A. Antigens that are expressed on tumor cells but not on normal cells are called **tumor specific antigens**; some of these antigens are unique to individual tumors, whereas others are shared among tumors of the same type.

B. Tumor antigens that are also expressed on normal cells are called **tumor-associated antigens**; in most cases, these antigens are normal cellular constituents whose expression is aberrant or dysregulated in tumors.

# Tumor Antigens



# Tumor Antigens



## **II. According to molecular structure:**

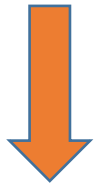
**The modern classification of tumor antigens is based on the molecular structure and source of antigens expressed by tumor cells that stimulate T cell or antibody responses in their hosts.**

# Tumor Antigens



**What are the sources of tumor specific antigens ?**

## **A. Tumor specific Antigens**



**Products of mutated:  
oncogenic viruses:**

**Protooncogene /Tumor suppressor gene**

**EBV HHV8 HPV**



**Products of**



# Tumor Antigens



## B. Tumor non specific Antigens: Oncofetal antigens

Genes encoding these proteins are:

Expressed during fetal life  
with malignant tumors

Silenced during development

Re-expressed



✓ **Antigens are present during normal fetal life, tumor cells but not on normal adult tissue**

# Carcinoembryonic Ag (CEA) & Alpha fetoptn (



**Carcinoembryonic antigen circulates at elevated levels in the serum of many patients with carcinoma of the colon, pancreas, breast, or liver. It is found in fetal gut, liver, and pancreas and in very small amounts in normal sera.**

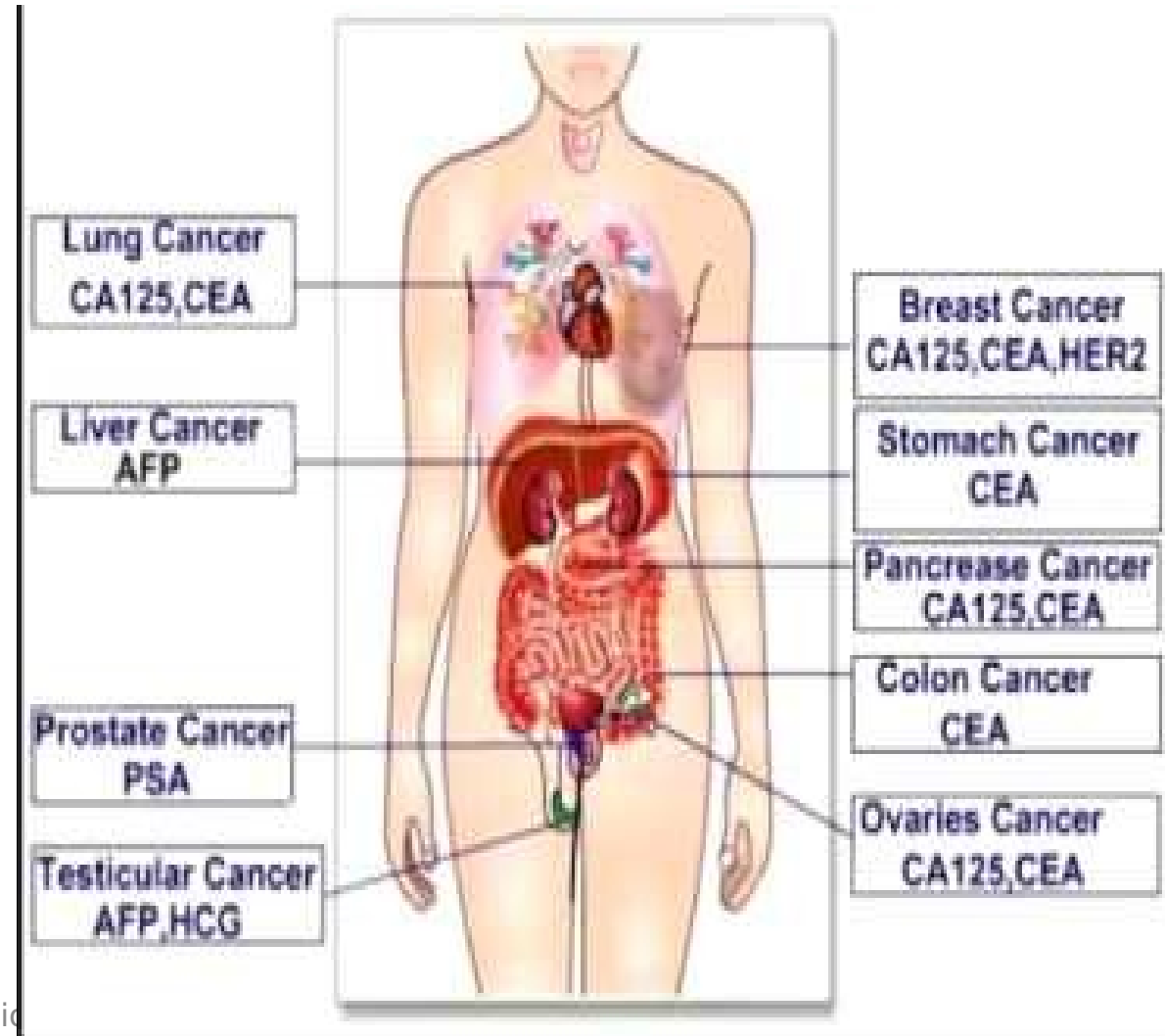
# Alpha fetoprotein



✓ Alpha fetoprotein is present at elevated levels in the sera of **hepatoma patients** and is used as a marker for this disease.

It is produced by fetal liver and is found in small amounts in some normal sera.

It is **nonspecific**; it occurs in several other malignant and nonmalignant diseases.



## Quiz: Tumor antigens



**Which of the following describes the behavior of tumor non-specific antigens?**

**a. Encoding genes are silenced in fetal life**

**b. Good prognostic marker**

**c. Products of mutated genes**

**d. Differ according to causative oncogenic virus**

**e. They cross react one another**



# Immune Surveillance

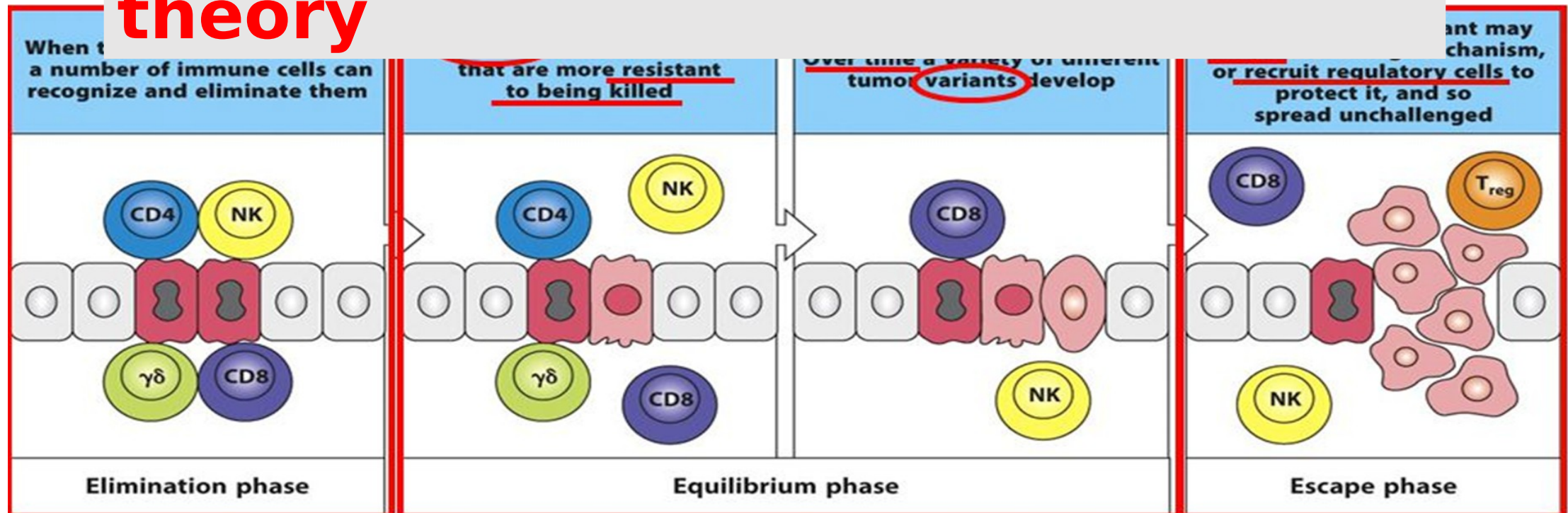


- Immune surveillance of cancer: a physiologic function of the immune system is to **recognize and destroy** clones of transformed cells before they grow into tumors and to kill tumors after they are formed.
- The existence of immune surveillance has been demonstrated by the increased incidence of some types of tumors in immunocompromised experimental animals and humans.



# Immune Surveillance

## Describe the immune surveillance theory



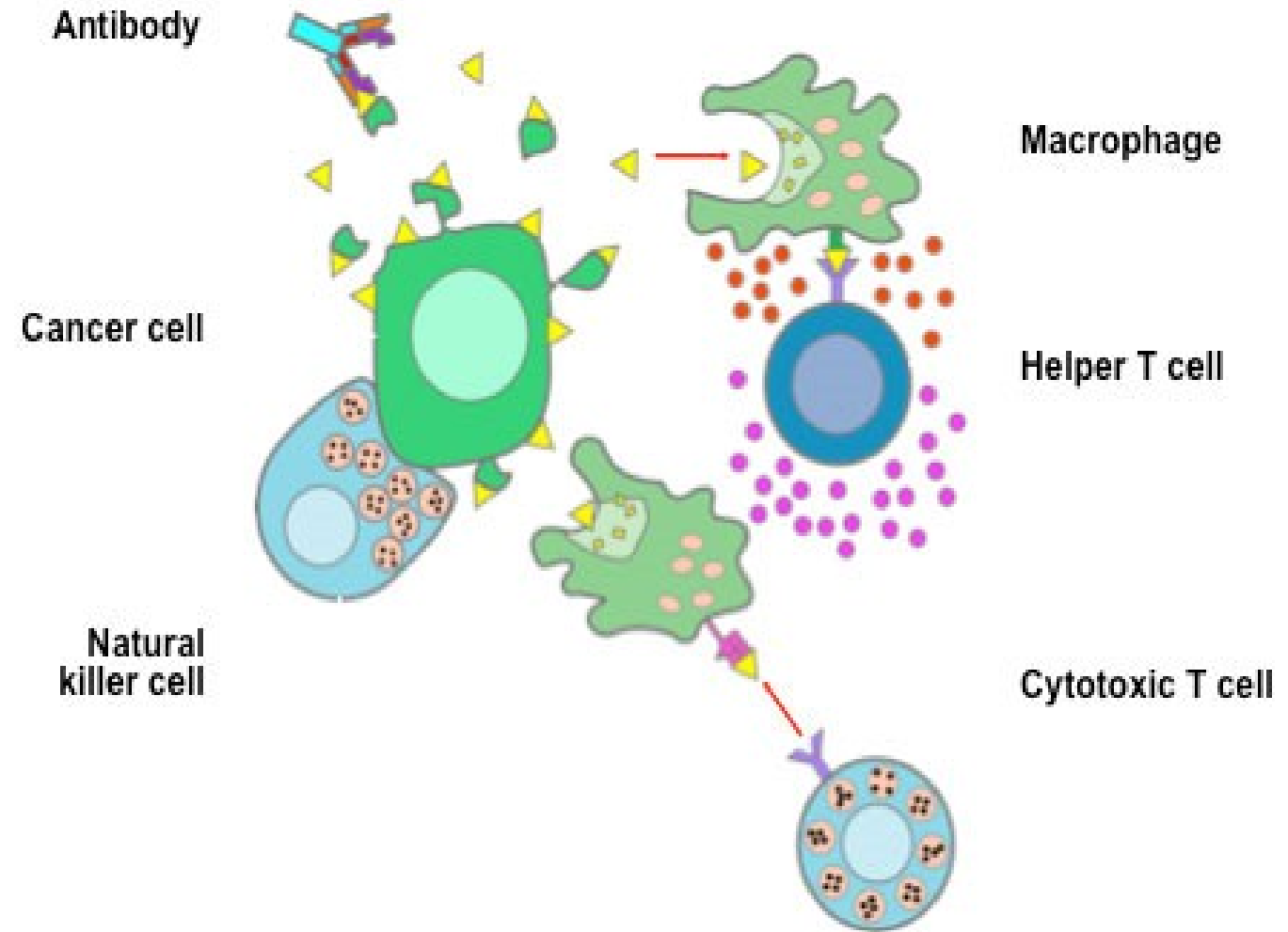
# Immune response against tumor cells



**Both innate and adaptive immune responses can be detected in patients and experimental animals, and various immune mechanisms can kill tumor cells in vitro.**

## **I. Innate IR:**

**A. Natural killer (NK) cells, which act without antibody**





# Immune response against tumor cells

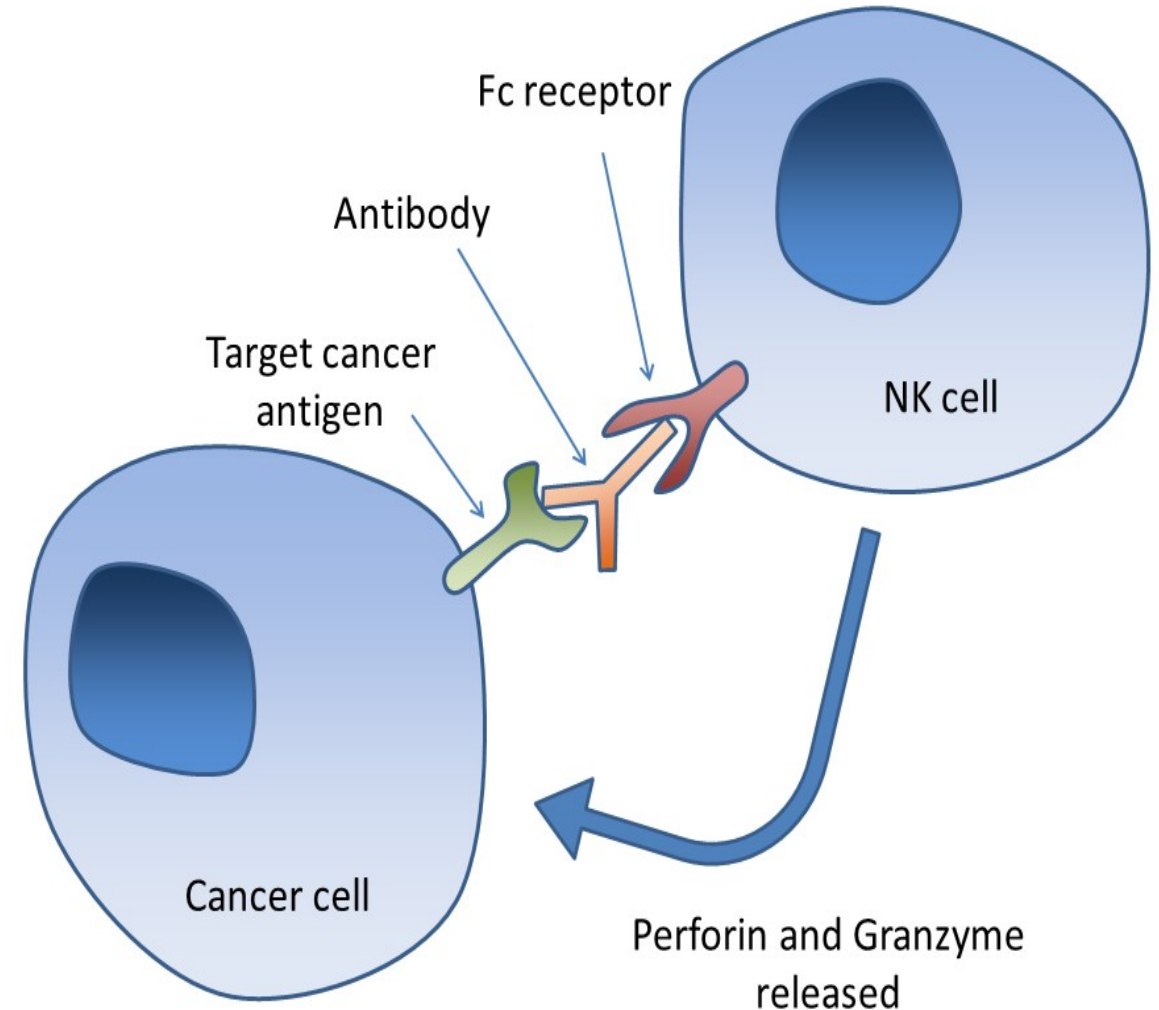


## II. Adaptive IR:

### A. Humoral: Antibodies:

**Antibodies may kill tumor cells by:**

- ✓ activating complement
- ✓ antibody-dependent cell-mediated cytotoxicity (ADCC), in which Fc receptor-bearing NK cells mediate the killing.





# Immune response against tumor cells



## **B. The cell-mediated immune responses that affect tumor cells in vitro include:**

- 1. CD8 cytotoxic T lymphocyte**
- 2. Activated macrophages: are capable of both inhibiting and promoting the growth and spread of cancers, depending on their activation state. Activation of macrophages by IFN- $\gamma$  produced by tumor-specific T cells**

# Quiz: Immune Surveillance



• How can your immune system kill a tumor cell?

a. Immunoglobulins

b. T helper cells

c. T regulatory cells

d. NK cells

e. Antibody dependent cell mediated cytotoxicity



# **Tumor evasion of Immune response [Escape phenomenon]**

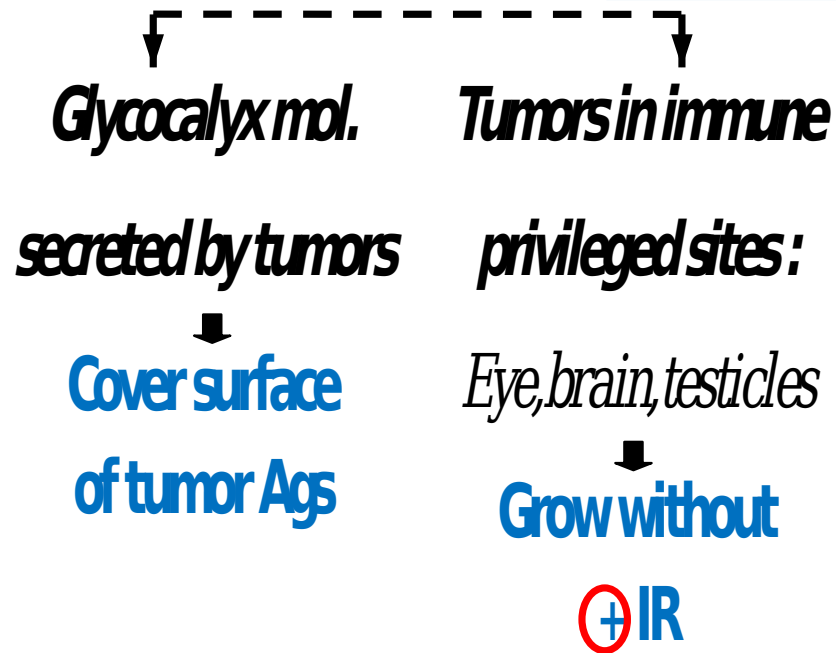
**Tumor Ags related  
Inappropriate T cell stimulation  
Immune Suppression by tumor  
Host factors**

# Tumor evasion of Immune response



## I. Tumor Ag related factors

### A. -Hidden tumor Ag



### B.

**Non cytotoxic Ab bind tumor Ag**

**mask antigens from cytotoxic T lymphocytes**

### C. Lost tumor Ags

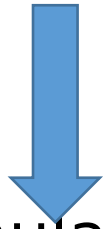


# Tumor evasion of Immune response



## II. Inappropriate T cell stimulation

EITHER : **Rare expression of B7 molecules on most tumors**



Poor co-stimulation of CTLs

OR

**↓ MHC class I on most**

**tumor cells**

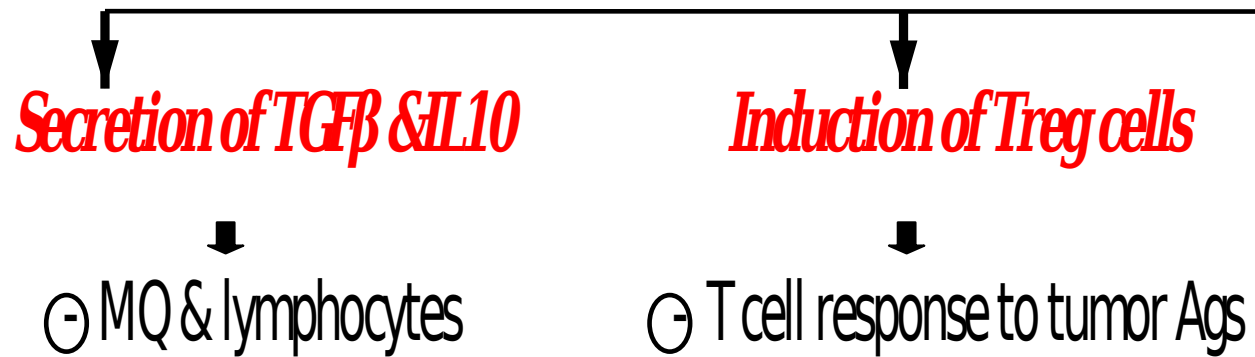


Not recognized by CTLs

# Tumor evasion of Immune response

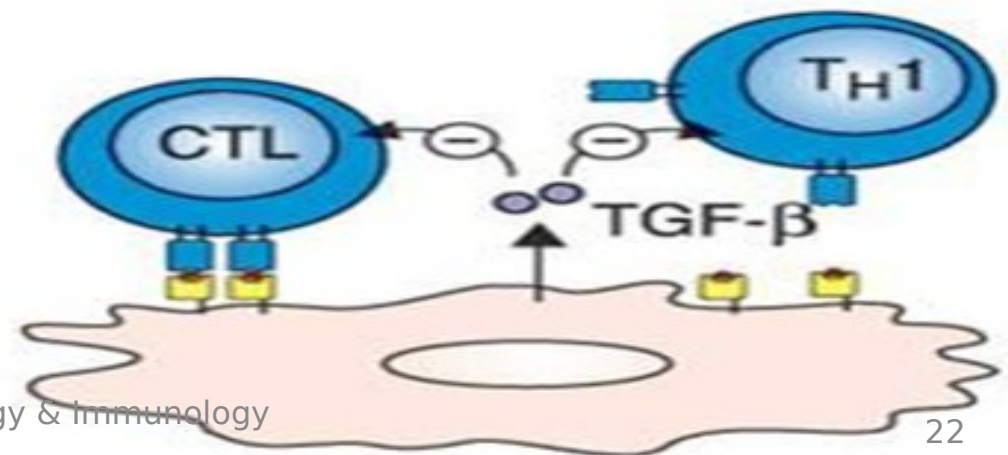


## Direct Immune suppression by tumors



### Tumor-induced immune suppression

Factors (e.g., TGF- $\beta$ ) secreted by tumor cells inhibit T cells directly



# Tumor evasion of Immune response



## IV. Host related factors

↓immunity due to

**Acquired  
Immune  
deficiency  
Syndrome  
(AIDS)**

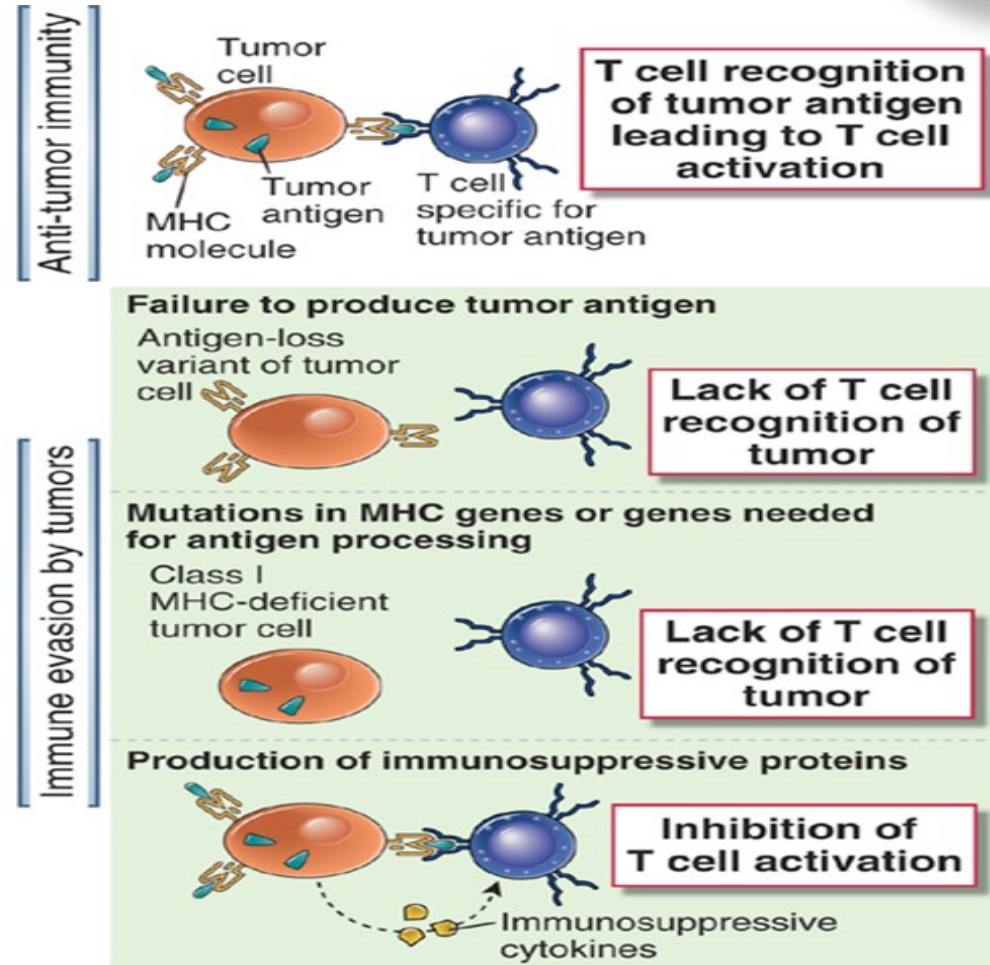
**Immune Suppressive  
drugs**  
↓  
**Treatment  
of  
autoimmu  
ne disease**

Prevention of  
graft rejection

***Extremes of age***

**Immatur  
e or  
exhaust  
ed  
Immune  
system**

# To sum up!!!



Abbas et al: Cellular and Molecular Immunology, 7e.  
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# Tumor Immune therapy



**Explain methods of specific & Non specific immune stimulation in immune theory.**

## **I. Non-specific stimulation of the immune system by the use of immunomodulators:**

either bacterial products e.g. BCG, or eukaryotic cell products e.g. thymic hormones and cytokines (IL-2 and IFNs).

## **II. Active Immunization:**

A. Using vaccines prepared from treated tumor cells or purified tumor antigens after reduction of tumor mass by surgery or radiotherapy.

# Tumor Immune therapy



B. Immunization with DNA encoding foreign MHC Ags into the tumor leading to expression of alloantigen (foreign MHC) creating an immune response against both alloantigens and tumor antigens

**III. Passive Immunotherapy : A.** Adoptive cellular immunotherapy:

**1. The use of tumor-infiltrating lymphocytes (TIL):** Some cancers are infiltrated by lymphocytes (NK cells and cytotoxic T cells) that seem likely to be trying to destroy the cancer cells.

**2. Lymphocytes activated by interleukin-2 (lymphokine-activated killer [LAK] cells)**

# Tumor Immune therapy



## **B. Therapeutic monoclonal antibodies:**

- 1. Monoclonal antibodies directed against CTLA-4 (inhibitor of costimulatory response) enhance the immune response against tumors**
- 2. Monoclonal antibodies directed against new surface antigens on malignant cells (e.g., B-cell lymphomas) can be useful in diagnosis.**

# Tumor Immune therapy



**3. Monoclonal antibodies coupled to toxins, such as diphtheria toxin or ricin, a product of the Ricinus plant, can kill tumor cells in vitro and may be useful for cancer therapy prospectively.**

## **IV. Genetic Manipulation of Tumor Cells:**

**By introduction of cytokine genes coding for IL-2, TNF, IFN- $\gamma$ , GM-CSF or coding for costimulatory molecules e.g. B7.1 and B7.2.**

# Tumor Immune therapy



## Unleashing the power of the immune system to defeat cancer

Immunotherapy — a medical treatment that mobilizes the body's own natural defense system to fight diseases — is revolutionizing the way we treat cancer. There are several different immunotherapy approaches that treat a variety of cancers. Some are approved for use; others are being tested in clinical trials.

### FIVE TYPES OF CANCER IMMUNOTHERAPY



#### Cellular therapy

The transfer of human cells to replace diseased cells with healthy, functional ones. Stem cell transplant and chimeric antigen receptor (CAR) T-cell therapy are examples of cellular therapies.



#### Immunomodulators

Medications that regulate and boost parts of the immune system. Checkpoint inhibitors and cytokines are immunomodulators.



#### Oncolytic virus therapy

Lab-modified viruses that infect and kill cancer cells without harming normal cells. Some of the viruses are found in nature, while others are modified in a lab.



#### Monoclonal antibodies

Man-made proteins that attack a specific part of a cancer cell. Some monoclonal antibodies are described as targeted therapies.



#### Cancer treatment vaccines

Medicines that train the immune system to recognize and destroy cancer cells. Unlike cancer prevention vaccines, these are designed for people who already have cancer.

# Quiz: Immune evasion by tumor cells



**How can inappropriate T cell stimulation play a role in immune evasion by tumor cells?**

- a. Rare expression of B7 molecules on most tumors**
- b. Massive co-stimulation of CTLs**
- c. Increased expression of MHC class I on most tumor cells**
- d. Poor expression of MHC II on all tumor cells**
- e. Masking antigens from cytotoxic T lymphocytes**





- 1. Tumors develop new antigens on cells either specific or non specific**
- 2. The immune system combat tumor via series of sequences summarized in the immune surveillance theory**
- 3. Both humoral & cell mediated immune response are acting against tumors**
- 4. Tumors exploit many mechanisms to escape the immune system armory**
- 5. Immune therapy modalities are promising in tumor management**

# Suggested Text Books



- 1. Review of Medical Microbiology and Immunology, Warren Levinson Chapter 68 p. 1236: 1249***
- 2. Cellular and molecular Immunology , Abul Abbas & Lichtmann, 2015, Chapter 18 p.383:397***



THANK  
YOU

